

That which is claimed is:

1. A microcapsule containing biologically active materials therein, the microcapsule comprising an ionically crosslinkable biocompatible gellable material, wherein at least the outer layer of said biocompatible gellable material is covalently crosslinked and optionally polyionically crosslinked, but not ionically crosslinked.
2. The microcapsule according to claim 1, wherein the core of said microcapsule is ionically crosslinked.
3. The microcapsule according to claim 2, wherein the core of said microcapsule is covalently crosslinked.
4. The microcapsule according to claim 1, wherein the core of said microcapsule is covalently crosslinked.
5. The microcapsule according to claim 4, wherein the core of said microcapsule is not ionically crosslinked.
6. The microcapsule according to claim 1, wherein the core of said microcapsule is not ionically crosslinked.

7. A macrocapsule containing biologically active materials therein, said macrocapsule comprising a first biocompatible gellable material which is ionically crosslinkable and which optionally contains at least one microcapsule therein, wherein, when at least one microcapsule is present, each microcapsule comprises a second biocompatible gellable material containing the biologically active materials therein and at least the outer layer of said macrocapsule is covalently crosslinked or polyionically crosslinked or both polyionically crosslinked and covalently crosslinked, but not ionically crosslinked, and wherein, when microcapsules are not present, at least the outer layer of said first biocompatible gellable material is covalently crosslinked and optionally polyionically crosslinked, but not ionically crosslinked.

8. The macrocapsule according to claim 7, wherein the core of said macrocapsule is ionically crosslinked.

9. The macrocapsule according to claim 8, wherein the core of said macrocapsule is covalently crosslinked.

10. The macrocapsule according to claim 7, wherein the core of said macrocapsule is covalently crosslinked.

11. The macrocapsule according to claim 10, wherein the core of said macrocapsule is not ionically crosslinked.

12. The macrocapsule according to claim 7, wherein the core of said macrocapsule is not ionically crosslinked.

13. The macrocapsule according to claim 7, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.

14. The macrocapsule according to claim 13, wherein the core of each of said microcapsules is covalently crosslinked.
15. The macrocapsule according to claim 8, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.
16. The macrocapsule according to claim 15, wherein the core of each of said microcapsules is covalently crosslinked.
17. The macrocapsule according to claim 9, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.
18. The macrocapsule according to claim 17, wherein the core of each of said microcapsules is covalently crosslinked.
19. The macrocapsule according to claim 10, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.
20. The macrocapsule according to claim 19, wherein the core of each of said microcapsules is covalently crosslinked.
21. The macrocapsule according to claim 11, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.
22. The macrocapsule according to claim 21, wherein the core of each of said microcapsules is covalently crosslinked.
23. The macrocapsule according to claim 12, wherein at least the outer layer of each of said microcapsules is covalently crosslinked.

24. The macrocapsule according to claim 23, wherein the core of each of said microcapsules is covalently crosslinked.

25. A delivery system for biologically active materials comprising a microcapsule according to claim 1, wherein said biologically active material is selected from the group consisting of living cells, biological materials, pharmacologically active drugs, and diagnostic agents.

26. The delivery system according to claim 25, wherein said biologically active material comprises living cells.

27. The delivery system according to claim 26, wherein said living cells are selected from the group consisting of pancreatic islet cells, tumor cells, human T-lymphoblastoid cells, islet of Langerhans cells, dopamine secreting cells, nerve growth factor cells, hepatocytes, adrenalin/angiotensin secreting cells, parathyroid cells, and norepinephrine/metencephalin secreting cells.

28. The delivery system according to claim 25, wherein said biologically active material comprises biological materials.

29. The delivery system according to claim 25, wherein said biologically active material comprises pharmacologically active drugs.

30. The delivery system according to claim 25, wherein said biologically active material comprises diagnostic agents.

31. The delivery system according to claim 25, wherein said biologically active material comprises pancreatic islet cells.

32. A delivery system for biologically active materials comprising a macrocapsule according to claim 7, wherein said biologically active material is selected from the group consisting of living cells, biological materials, pharmacologically active drugs, and diagnostic agents.

33. The delivery system according to claim 32, wherein said biologically active material comprises living cells.

34. The delivery system according to claim 33, wherein said living cells are selected from the group consisting of pancreatic islet cells, tumor cells, human T-lymphoblastoid cells, islet of Langerhans cells, dopamine secreting cells, nerve growth factor cells, hepatocytes, adrenalin/angiotensin secreting cells, parathyroid  
5 cells, and norepinephrine/metencephalin secreting cells.

35. The delivery system according to claim 32, wherein said biologically active material comprises biological materials.

36. The delivery system according to claim 32, wherein said biologically active material comprises pharmacologically active drugs.

37. The delivery system according to claim 32, wherein said biologically active material comprises diagnostic agents.

38. The delivery system according to claim 32, wherein said biologically active material comprises pancreatic islet cells.

39. A method of making a microcapsule containing biologically active materials therein and having substantially no ionic crosslinking in at least the outer layer thereof, said method comprising:subjecting a microcapsule which contains biologically active materials therein, wherein at least the outer layer thereof is 5 ionically crosslinked, and wherein at least the outer layer thereof is covalently crosslinked and optionally polyionically crosslinked, to conditions sufficient to disrupt ionic crosslinking in at least the outer layer thereof, thereby forming a microcapsule having substantially no ionic crosslinking in at least the outer layer thereof.

40. A method of making a macrocapsule containing biologically active materials therein and having substantially no ionic crosslinking in at least the outer layer thereof, said method comprising:subjecting a macrocapsule which contains 5 biologically active materials therein, optionally contained within at least one optionally present microcapsule, wherein at least the outer layer of the macrocapsule is ionically crosslinked, and wherein when microcapsules are not present, at least the outer layer of the macrocapsule is covalently crosslinked and optionally polyionically crosslinked, andwhen at least one microcapsule is present, at least the outer layer of 10 the macrocapsule is covalently crosslinked or polyionically crosslinked or both covalently crosslinked and polyionically crosslinked,to conditions sufficient to disrupt ionic crosslinking in at least the outer layer thereof, thereby forming a macrocapsule having substantially no ionic crosslinking in at least the outer layer thereof.

41. A method of making a microcapsule containing biologically active materials therein, said method comprising simultaneously subjecting a droplet comprising a suspension of biologically active materials in a covalently crosslinkable carrier to conditions sufficient to prevent substantial dissociation thereof, and 5 subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking thereof, thereby forming the microcapsule.

42. The method of claim 41, wherein subjecting the droplet to conditions sufficient to prevent substantial dissociation thereof comprises contacting the droplet with a medium which is substantially immiscible with the droplet and which does not substantially inhibit the induction of covalent crosslinking.

43. The method of claim 42, wherein the droplet is aqueous and the medium is selected from the group consisting of soybean oil, coconut oil, safflower oil, sunflower oil, and sesame oil.

44. The method of claim 42, wherein the droplet is aqueous and the medium comprises soybean oil.

45. The method of claim 42, wherein subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking comprises irradiating the droplet with sufficient energy to induce photocrosslinking of the covalently crosslinkable carrier.

46. The method of claim 43, wherein subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking comprises contacting the droplet with light from high pressure mercury lamps for a time sufficient to induce photocrosslinking of the covalently crosslinkable carrier.

47. A method of making a macrocapsule containing biologically active materials therein, said method comprising simultaneously subjecting a droplet comprising a suspension of a plurality of microcapsules containing the biologically active materials in a covalently crosslinkable carrier to conditions sufficient to prevent  
5 substantial dissociation thereof, and subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking thereof, thereby forming the macrocapsule.

48. The method of claim 47, wherein subjecting the droplet to conditions sufficient to prevent substantial dissociation thereof comprises contacting the droplet with a medium which is substantially immiscible with the droplet and which does not substantially inhibit the induction of covalent crosslinking.

49. The method of claim 48, wherein the droplet is aqueous and the medium is selected from the group consisting of soybean oil, coconut oil, safflower oil, sunflower oil, and sesame oil.

50. The method of claim 48, wherein the droplet is aqueous and the medium comprises soybean oil.

51. The method of claim 48, wherein subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking comprises irradiating the droplet with sufficient energy to induce photocrosslinking of the covalently crosslinkable carrier.

52. The method of claim 50, wherein subjecting the droplet to conditions sufficient to induce substantial covalent crosslinking comprises contacting the droplet with light from high pressure mercury lamps for a time sufficient to induce photocrosslinking of the covalently crosslinkable carrier.

53. A microcapsule containing at least one cell aggregate therein, said microcapsule having a core which is not ionically crosslinked and an outer layer, wherein at least the outer layer of the microcapsule is covalently crosslinked or polyionically crosslinked or both covalently crosslinked and polyionically crosslinked, but not ionically crosslinked, and wherein said at least one cell aggregate is contained within the core.



54. A macrocapsule containing at least one cell aggregate therein, said macrocapsule comprising a first biocompatible gellable material which is covalently crosslinkable and which contains at least one microcapsule therein, wherein each microcapsule comprises a second biocompatible gellable material which is ionically crosslinkable, wherein at least the outer layer of the macrocapsule is covalently crosslinked or polyionically crosslinked or both polyionically crosslinked and covalently crosslinked, wherein at least the outer layer of the microcapsule(s) is covalently crosslinked or polyionically crosslinked or both polyionically crosslinked and covalently crosslinked, and wherein the core of the microcapsule(s) is not ionically crosslinked and contains said at least one cell aggregate.

55. A macrocapsule containing at least one cell aggregate therein, said macrocapsule comprising a first biocompatible gellable material which is ionically crosslinkable and covalently crosslinkable and which optionally contains at least one microcapsule therein, wherein each microcapsule comprises a second biocompatible gellable material which is ionically crosslinkable, wherein at least the outer layer of the macrocapsule is covalently crosslinked or polyionically crosslinked or both polyionically crosslinked and covalently crosslinked, and wherein the core of the macrocapsule is not ionically crosslinked and contains said at least one cell aggregate.

56. A method of making a microcapsule containing at least one cell aggregate therein, said method comprising

subjecting a microcapsule comprising an ionically crosslinked biocompatible gellable material wherein at least the outer layer of the microcapsule is covalently crosslinked or polyionically crosslinked or both polyionically crosslinked and covalently crosslinked, wherein said microcapsule encapsulates at least one individual cell(s), to conditions sufficient to disrupt ionic crosslinking within the core of the microcapsule, thereby facilitating proliferation and/or aggregation of said individual cells to form at least one cell aggregate within the microcapsule.

57. The method of claim 56, said method further comprising  
 subjecting the microcapsule to conditions sufficient to promote  
 proliferation of the at least one individual cell(s) after subjecting the microcapsule to  
 conditions sufficient to disrupt ionic crosslinking within the core of the microcapsule.

58. The method of claim 56, said method further comprising  
 subjecting the microcapsule to conditions sufficient to promote  
 proliferation of the at least one individual cell(s) before subjecting the microcapsule to  
 conditions sufficient to disrupt ionic crosslinking within the core of the microcapsule.

59. A method of making a macrocapsule containing at least one cell  
 aggregate therein, said method comprising

subjecting a macrocapsule comprising a first biocompatible gellable  
 material and at least one microcapsule therein, wherein at least the outer layer of the  
 5 macrocapsule is covalently crosslinked or polyionically crosslinked or both  
 polyionically crosslinked and covalently crosslinked, wherein each of the  
 microcapsules comprises a second biocompatible gellable material which is ionically  
 crosslinked and which encapsulates at least one individual cell, wherein at least the  
 outer layer of the at least one microcapsule is covalently crosslinked or polyionically  
 10 crosslinked or both polyionically crosslinked and covalently crosslinked, to conditions  
 sufficient to disrupt ionic crosslinking within the core of the at least one  
 microcapsule, thereby facilitating proliferation and/or aggregation of said at least one  
 individual cell to form at least one cell aggregate within the core of the  
 microcapsule(s).

60. The method of claim 59, said method further comprising  
subjecting the macrocapsule to conditions sufficient to promote  
proliferation of said at least one individual cell after subjecting the macrocapsule to  
conditions sufficient to disrupt ionic crosslinking within the core of the at least one  
5 microcapsule.

61. The method of claim 59, said method further comprising  
subjecting the macrocapsule to conditions sufficient to promote  
proliferation of said at least one individual cell before subjecting the macrocapsule to  
conditions sufficient to disrupt ionic crosslinking within the core of the at least one  
5 microcapsule.

62. A method of making a macrocapsule containing at least one cell  
aggregate therein, said method comprising  
subjecting a macrocapsule comprising a first biocompatible gellable  
material and at least one individual cell encapsulated therein, optionally contained  
5 within at least one optionally present microcapsule therein, wherein at least the outer  
layer of the macrocapsule is covalently crosslinked or polyionically crosslinked or  
both polyionically crosslinked and covalently crosslinked, wherein each of the  
microcapsules comprises a second biocompatible gellable material which is ionically  
crosslinkable, to conditions sufficient to disrupt ionic crosslinking within  
10 microcapsule and at least the core of the macrocapsule, thereby facilitating  
proliferation and/or aggregation of said individual pancreatic islet cells to form at least  
one cell aggregate within the core of the macrocapsule.

63. The method of claim 62, said method further comprising  
subjecting the macrocapsule to conditions sufficient to promote  
proliferation of the at least one individual cell after subjecting the macrocapsule to  
conditions sufficient to disrupt ionic crosslinking within the microcapsule and at least  
5 the core of the macrocapsule.

64. The method of claim 62, said method further comprising  
subjecting the macrocapsule to conditions sufficient to promote  
proliferation of the at least one individual cell before subjecting the macrocapsule to  
conditions sufficient to disrupt ionic crosslinking within the microcapsule and at least  
5 the core of the macrocapsule.

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